RESEARCH

Associations between palliative chemotherapy and adult cancer patients' end of life care and place of death: prospective cohort study

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Abstract

Objectives To determine whether the receipt of chemotherapy among terminally ill cancer patients months before death was associated with patients' subsequent intensive medical care and place of death.

Design Secondary analysis of a prospective, multi-institution, longitudinal study of patients with advanced cancer.

Setting Eight outpatient oncology clinics in the United States.

Participants 386 adult patients with metastatic cancers refractory to at least one chemotherapy regimen, whom physicians identified as terminally ill at study enrollment and who subsequently died.

Main outcome measures Primary outcomes: intensive medical care (cardiopulmonary resuscitation, mechanical ventilation, or both) in the last week of life and patients' place of death (for example, intensive care unit). Secondary outcomes: survival, late hospice referrals (≤1 week before death), and dying in preferred place of death.

Results 216 (56%) of 386 terminally ill cancer patients were receiving palliative chemotherapy at study enrollment, a median of 4.0 months before death. After propensity score weighted adjustment, use of chemotherapy at enrollment was associated with higher rates of cardiopulmonary resuscitation, mechanical ventilation, or both in the last week of life (14% *v* 2%; adjusted risk difference 10.5%, 95% confidence interval 5.0% to 15.5%) and late hospice referrals (54% *v* 37%; 13.6%, 3.6% to 23.6%) but no difference in survival (hazard ratio 1.11, 95% confidence interval 0.90 to 1.38). Patients receiving palliative chemotherapy were more likely to die in an intensive care unit (11% *v* 2%; adjusted risk difference 6.1%, 1.1% to 11.1%) and less likely to die at home (47% *v* 66%; –10.8%, –1.0% to –20.6%), compared with those who were not. Patients receiving palliative chemotherapy were also less likely to die in their preferred place, compared with those who were not (65% *v* 80%; adjusted risk difference –9.4%, –0.8% to –18.1%).

Conclusions The use of chemotherapy in terminally ill cancer patients in the last months of life was associated with an increased risk of undergoing cardiopulmonary resuscitation, mechanical ventilation or both and of dying in an intensive care unit. Future research should determine the mechanisms by which palliative chemotherapy affects end of life outcomes and patients' attainment of their goals.

Introduction

Chemotherapy is used to treat metastatic cancer, with the goal of palliating symptoms and improving survival. Between 20% and 50% of patients with incurable cancers receive chemotherapy within 30 days of death,[1 2] despite growing concerns that it may not be effective. Recently, the American Society for Clinical Oncology identified end of life chemotherapy as one of the "top five" practices that could improve patients' care and reduce costs, if stopped.[3] Deciding when to discontinue chemotherapy is often challenging, however, given limited data on whether chemotherapy is helpful or harmful in the final months of life.[2-5]

Research suggests that the use of chemotherapy within two weeks of death is associated with lower rates of hospice use,[6 7] but only 6.2% of patients receive chemotherapy this late.[8] Most decisions about treatment occur months before death, when data to guide decision making about chemotherapy are more limited. For example, in a randomized controlled study comparing early palliative care integrated with oncology care versus standard oncology care among patients newly diagnosed as having metastatic lung cancer, Greer et al found that 62% of all enrolled

patients received chemotherapy within two months of death.[9] [10] However, patients who received concurrent palliative and oncologic care stopped intravenous chemotherapy an average of two months earlier than did those in the standard oncology group but had a longer median overall survival and were more likely to receive at least one week of hospice services.[9] [10] To our knowledge, however, Greer at al's study and others have not specifically examined whether the use of chemotherapy in the months leading up to the patient's death is associated with the subsequent receipt of intensive medical care in the last week of life or death in an intensive care unit.

In this secondary analysis of Coping with Cancer data,[11] we sought to determine whether terminally ill cancer patients who were receiving chemotherapy at study enrollment were more likely to receive intensive medical care in the last week of life and die in an intensive care unit, compared with those who were not. We hypothesized that palliative chemotherapy would be associated with more intensive medical care (for example, cardiopulmonary resuscitation, mechanical ventilation, or both) and late referrals to a hospice, as chemotherapy is often an exclusion criterion for hospice admission,[12] [13] and oncologists express reluctance about discussing advance care planning while prescribing chemotherapy.[14-16] Similarly, we expected that patients receiving palliative chemotherapy would be less likely to die where they wanted to, as oncologists often delay discussing patients' preferred site of death, compared with other non-cancer specialists.[14]

Methods

Coping with Cancer was a federally funded, prospective, longitudinal, multi-institution cohort study of terminally ill cancer patients and their informal caregivers, which was designed to examine how psychosocial factors influence patients' medical care and caregivers' adjustment to bereavement.[11] Of 917 eligible patients, 638 (69.6%) consented and enrolled in Coping with Cancer. The three most common reasons for non-participation were "not interested" (n=120), "other" (n=69), and "caregiver refuses" (n=37). Participants were more likely than non-participants to be Hispanic (12% (75/638) *v* 6% (16/279), P=0.006), but otherwise did not differ by sociodemographic characteristics.

This report describes 386 patients who were recruited between October 2002 and February 2008 and died during the course of the study, such that we could analyze their end of life medical care. We excluded participants in clinical trials (n=37), as their treatment preferences and therapeutic expectations often differ from those of patients receiving standard chemotherapy or supportive care.[17] Patients who had died as of February 28, 2008 did not differ significantly in type of cancer or receipt of chemotherapy from participants who lived. However, decedents had worse performance status, more symptoms, and greater awareness of terminal illness and were more likely to be male, unmarried, uninsured, less educated, younger, and non-white (all P<0.05).

Participating sites included Yale Cancer Center, the Veterans Affairs Connecticut Healthcare System Comprehensive Cancer Clinics, the Parkland Hospital Palliative Care Service, Simmons Comprehensive Cancer Center, Massachusetts General Hospital, Dana-Farber Cancer Institute, Memorial Sloan Kettering Cancer Center, and New Hampshire Oncology-Hematology. The Dana-Farber/Harvard Cancer Center's Office for Human Research Studies coordinated the study, and all patients provided written informed consent.

Patients were eligible to participate if they had metastatic cancer that had progressed through at least one chemotherapy regimen, had a physician formulated prognosis of six months or less to live, were aged at least 20 years, had an informal caregiver, and were assessed by clinic staff and interviewer as having adequate stamina to complete the interview. We excluded patient-caregiver dyads in which either the patient or the caregiver refused to participate, met criteria for dementia or delirium (by neurobehavioral cognitive status examination), or did not speak either English or Spanish.

Patients participated in a baseline interview in English or Spanish for a $25 (£15; €18) payment at a time that was close to when decisions about chemotherapy were being made. We reviewed medical charts at the time of study enrollment and recorded current use of chemotherapy. Research assistants confirmed patients' performance status and prognosis of six months or less with physicians. We did not record the number and length of previous and subsequent treatments. After each patient's death, we conducted a chart review and postmortem interview with the patient's caregivers to confirm the medical care received at the end of life, the patient's place of death, and whether the patient died in his or her preferred place of death.

Main outcome measures

The primary outcomes were end of life treatment and location of death. We determined use of intensive interventions in the last week of life (that is, cardiopulmonary resuscitation, mechanical ventilation, or both) and location of death (intensive care unit, hospital, nursing home, inpatient hospice, or home) through a medical chart review and interviews with caregivers.

Secondary outcome measures

Survival—We abstracted the time from study enrollment to death from medical charts.

Late hospice referrals—We determined the duration of hospice services through chart review and interviews with caregivers. We defined late referrals to a hospice as one week or less before death.[11]

Attainment of preferred place of death—In postmortem interviews, we asked caregivers, "Do you think that the place of death was where the patient would have most wanted to die?" Patients whose caregivers responded "yes" were designated as having died where they wanted to.

Primary independent variable of interest

We reviewed medical charts on study enrollment to determine whether patients were receiving chemotherapy, radiation, pain management, or treatment on a clinical trial at the time of enrollment. Patients receiving chemotherapy as any part of their treatment, outside of a clinical trial, were included in the chemotherapy group.

Additional covariates measured at baseline

Sociodemographic characteristics—Patients reported sex, age, marital status, race/ethnicity, religion, health insurance coverage, and last grade completed in school.

Health status measures—We measured patients' functional status with the Karnofsky score and Eastern Cooperative Oncology Group (ECOG) performance status,[18] comorbid medical conditions with the Charlson Comorbidity Index,[19] and quality of life with the McGill Quality of Life Index.[20].

Treatment preferences, terminal illness acknowledgment, coping, communication, and advance care planning—We used validated

measures to elicit patients' preferences for chemotherapy, mechanical ventilation, admission to an intensive care unit near death, and life extending care versus comfort care.[21] [22] We also assessed patients' acknowledgment of terminal illness, as this has been associated with higher rates of advance care planning and hospice use.[23] The Brief COPE and RCOPE surveys assessed active, emotion focused, maladaptive, and positive religious coping with cancer related stress.[24] We also asked patients whether they recalled having an end of life discussion with their physician,[11] had a strong therapeutic alliance with their providers,[25] and had completed a living will, durable power of attorney, or do not resuscitate order (see web appendix).

Statistical analyses

We used *t* test, χ^2, and Fisher's exact statistics, as appropriate, to test for significant associations between patients' baseline characteristics and the receipt of chemotherapy at study enrollment. We used multiple imputation to impute missing data for items other than the dependent variables (for which no data were missing in our cohort)[26]; item non-response was less than 14% for all variables.

We used propensity score analyses to assess the association between patients who were or were not receiving chemotherapy at the time of enrollment.[27] To do the propensity score analysis, we first used logistic regression to assess the association of all measured demographic, clinical, psychosocial, and institutional characteristics with being treated with chemotherapy at baseline. The model included age, sex, marital status, insurance status, education, race/ethnicity, religion, institution, cancer type, Karnofsky and ECOG scores, Charlson Comorbidity Index, McGill Quality of Life Index subscales, patients' treatment preferences and advance care planning, terminal illness acknowledgment, therapeutic alliance with physicians, end of life discussions, and coping styles. For each patient, we used the regression coefficients and the observed covariates to calculate the propensity to receive chemotherapy at study enrollment and derived individual weights equal to the probability of belonging to the opposite group (that is, not receiving chemotherapy).[11] [28] Thus, after propensity adjustment the weighted distribution of characteristics in both groups were balanced. We then used a generalized linear regression model with an identity link function and a binomial distribution, with the propensity weighted cohorts, to estimate the association of chemotherapy with binary outcomes (for example, cardiopulmonary resuscitation and/or mechanical ventilation). Our events were rare, so we calculated and reported our results as adjusted risk differences as odds ratios may exaggerate the actual risk. We did a sensitivity analysis to examine the effect of excluding covariates that might change over time (Karnofsky score, ECOG score, McGill Quality of Life scales, treatment preferences, and terminal illness awareness), as the exact date of starting palliative chemotherapy was not ascertained during the baseline assessment. We used Cox proportional hazard models to compare the overall survival of patients who were receiving palliative chemotherapy with those who were not, with adjustment for propensity weights.

We used SOLAS for Missing Data Analysis version 4.0 for multiple imputation and SAS version 9.2 for statistical analyses. We present two sided P values without adjustment for multiple comparisons; we considered P<0.05 to be significant.

Results

The cohort consisted of 386 terminally ill cancer patients who died a median of 4.0 (interquartile range 1.8-8.3) months after enrollment in the study. Overall, 56.0% of participants were receiving palliative chemotherapy on study enrollment. As shown in table 1⇓, patients who were receiving palliative chemotherapy were more likely to be younger, married, insured, and better educated and to have better performance status, overall quality of life, physical functioning, and psychological wellbeing compared with patients who were not receiving chemotherapy (all P≤0.04). They were also more likely to express a preference to receive "life extending" care over comfort care (39% *v* 26%, P=0.01), including chemotherapy if it might extend their life by one week (86% *v* 60%, P<0.001), compared with those not receiving chemotherapy.

Patients receiving palliative chemotherapy were less likely to acknowledge that their illness was terminal (35% *v* 49%, P=0.04) and to report having discussed their end of life wishes with a physician (37% *v* 48%, P=0.03), compared with those who were not. They were also less likely to have completed a do not resuscitate order (36% *v* 49%, P<0.05). Propensity score weighting successfully balanced all of the observed differences in patients' characteristics between the two groups (table 1⇓).

In propensity score weighted analyses, receipt of chemotherapy at enrollment was associated with significantly more intensive medical interventions near death. As shown in table 2⇓, patients receiving palliative chemotherapy were more likely to receive cardiopulmonary resuscitation, mechanical ventilation, or both in the last week of life (14% *v* 2%; adjusted risk difference 10.5%, 95% confidence interval 5.0% to 15.5%) compared with those who were not. Chemotherapy use was also associated with higher rates of use of a feeding tube in the last week (11% *v* 5%; adjusted risk difference 7.1%, 1.7% to 12.5%) and of late hospice referrals (54% *v* 37% enrolled within one week of death; 13.6%, 3.6% to 23.6%). In adjusted Cox proportional hazards models, we found no significant difference in overall survival between patients who were receiving palliative chemotherapy at study enrollment and those who were not (hazard ratio 1.11, 95% confidence interval 0.90 to 1.38). In a secondary model, we assessed the association between receipt of palliative chemotherapy and the intensity of end of life medical care without including characteristics that might have changed since the decision to start palliative chemotherapy was made (that is, performance status, quality of life, treatment preferences, and terminal illness acknowledgment), and the results did not change.

As shown in table 3⇓, patients who received chemotherapy at enrollment were more likely to die in an intensive care unit (11% *v* 2%; adjusted risk difference 6.1%, 1.1% to 11.1%) and less likely to die at home (47% *v* 66%; −10.8%, −1.0% to −20.6%), compared with those who were not. Patients who were receiving palliative chemotherapy on study enrollment were also less likely die in their preferred place, compared with those who were not (68% *v* 80%; adjusted risk difference −9.4%, −0.8% to −18.1%). In a second model, we examined the association between palliative chemotherapy and patients' place of death without including characteristics that might change over time; our results were consistent, except that patients' likelihood of dying in their preferred place was no longer statistically significant (P=0.07).

Discussion

Our results suggest that terminally ill patients with advanced cancers who receive chemotherapy a few months before death are more likely to receive intensive care at the end of life, compared with patients who do not. In this study, the use of chemotherapy a median of 4.0 months before death was

associated with an increased risk of undergoing mechanical ventilation, cardiopulmonary resuscitation, or both in the last week of life and of being referred to a hospice late, both of which have been associated with worse quality of life for patients at the end of life,[11-30] more distress in bereaved caregivers,[11 29] and higher costs.[31] The use of palliative chemotherapy was also associated with an increased risk of dying in an intensive care unit, a decreased likelihood of dying at home, and a lower likelihood that patients died in their preferred place.

Comparison with other studies

This is the first study, to our knowledge, to examine the associations between the use of palliative chemotherapy and patients' location of death. Whereas previous studies have identified patient, caregiver, and system level factors that influence where cancer patients die,[32-34] few have focused on how the care that terminally ill cancer patients receive in the final months of life relates to their place of death outside of hospice or palliative care settings.[35]

In this study, only a minority of terminally ill cancer patients preferred life extending medical care over care that focused on relieving pain and discomfort. However, more than half wanted chemotherapy if it would extend their life by one week, including 60% of patients who were not receiving chemotherapy. This finding is consistent with previous studies that have shown that many cancer patients are willing to undergo significant treatment related toxicities for small objective benefits.[36 37] The one week survival threshold for chemotherapy that we observed is significantly lower than the four to five month thresholds previously reported in similar populations of patients,[37-39] and it suggests that cancer patients may not regard chemotherapy as burdensome because they are willing to receive it for very limited temporal pay-off.

Our findings also underscore the challenge that many oncologists face when discussing the option of stopping chemotherapy with patients and their caregivers,[40] particularly when patients—and physicians—may equate stopping treatment with "giving up" or "doing nothing."[41 42] In this study, we observed significant differences in the rates of use of chemotherapy by institution, although they were balanced after propensity weighting and therefore did not influence the observed associations between receipt of chemotherapy and patients' end of life medical care and place of death. Although our study could not directly compare the relative influences of patient, provider, and institution level factors, we suspect that a combination of these factors explains the differences observed. Future studies should examine the most important determinants of end of life use of chemotherapy.

In this study, we did not observe a difference in survival between patients who received palliative chemotherapy and those who did not. This should not be interpreted as evidence that palliative chemotherapy is futile in terminally ill cancer patients, as our analysis was limited to small sample of decedents and may have excluded patients who benefited most from chemotherapy. Instead, this finding should serve as a reminder that palliative chemotherapy does not necessarily extend life, but is associated with more intensive end of life care and increased risk of dying in an intensive care unit, so continuing treatment should not come at the cost of engaging in advance care planning.[14 15]

Strengths and limitations

This study has several important strengths. Previous studies have found that older patients who received chemotherapy within two weeks of death had higher rates of emergency department visits and hospital admissions and decreased hospice use at the end of life.[6-43] Our data, collected more than a decade later, extend these results by examining associations between palliative chemotherapy given months before death, at the time when most decision making about chemotherapy occurs, and the intensity of patients' end of life medical care and place of death. Our study may also be more representative of the care provided to "dying patients" than previous work because it enrolled patients of all ages who were prospectively identified by their physicians as terminally ill with a prognosis of six months or less to live.[44 45] In addition, we had comprehensive data on patients' performance status, physical functioning, quality of life, and many other psychosocial factors associated with end of life decision making, including patients' treatment preferences, awareness of terminal illness, and end of life discussions with physicians,[11-46] which are rarely available in other databases.

The study also has limitations. Most notably, we did not have any information about the timing or nature of patients' decisions about treatment after study enrollment, except for the last week of life. However, subsequent decisions to resume or stop chemotherapy would minimize differences between the two groups, making detection of the effects observed less likely. Despite this, we observed significant associations between the use of palliative chemotherapy and the intensity of patients' end of life care and place of death, and our results did not change when we removed characteristics that often change in response to chemotherapy (such as quality of life and performance status) or disease progression (such as treatment preferences and awareness of terminal illness). However, the association between receipt of palliative chemotherapy and patients' preferred place of death became marginally significant in sensitivity analyses and when we included additional covariates in propensity weighted models; thus, future studies should confirm these results in larger populations.

In addition, we did not have information about patients' baseline preferences for the timing of referral to a hospice or place of death. Although short hospice stays—and treatment in an intensive care unit near death—may be viewed as beneficial to dying patients or their family caregivers,[47] our previous work suggests that for most patients these outcomes are associated with worse quality of life for patients and more distress in family caregivers six months after bereavement.[11 29] In addition, we did not randomize patients to receive palliative chemotherapy or not. Whereas propensity score weighting can effectively adjust for observed differences, it can adjust for unobserved confounders only if they are associated with observed confounders. Furthermore, patients who were receiving chemotherapy at enrollment may have differed in unmeasured ways from those who were not receiving chemotherapy (for example, in their disease duration or previous experiences with chemotherapy).

Finally, our analyses were limited to deceased patients who died in 2008, and only a small proportion of our patients experienced the end of life outcomes of interest. Nevertheless, the frequency of events we observed is comparable to or higher than those from population based studies using the most recent Medicare claims available. For example, Teno et al found that 6.7% of cancer patients received mechanical ventilation in the last month of life in 2009.[48] In our study, 8.5% of terminally ill cancer patients received mechanical ventilation or cardiopulmonary resuscitation in the last week of life, but a significant difference existed between groups (13.9% v 1.6%) based on exposure to chemotherapy at baseline. Furthermore, we expect that our

findings may be a conservative estimate, as Teno et al also found that the intensity of medical care near death is increasing over time.[48]

Conclusions and policy implications

Our results suggest that less use of palliative chemotherapy among patients recognized to have a life expectancy of six months or less—or more frequent end of life discussions in this group—may reduce intensive end of life care and promote earlier access to hospice services, thus improving the quality of advanced cancer patients' end of life care. Future studies should determine the mechanisms by which palliative chemotherapy is associated with increased risk of receiving intensive care at the end of life and dying in an intensive care unit and examine explicitly whether palliative chemotherapy is associated with patients' goal attainment.

Our study has important implications for oncology providers, patients with advanced cancer, and caregivers facing decisions about treatment. It suggests that end of life discussions may be particularly important for patients receiving palliative chemotherapy, who should be informed by data on the likely outcomes associated with its use. The findings also suggest the need for oncology providers to elicit patients' preferred site of death to ensure that patients' end of life experiences are congruent with their values.

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What is already known on this topic

Many patients with metastatic cancer receive chemotherapy in the final months of life, but most are not provided with information on the likely effect on their survival, future care and quality of life, and location of death

Retrospective, population based studies suggest that cancer patients who receive chemotherapy within two weeks of death are less likely to receive hospice services, compared with those who do not

Few studies have examined prospectively whether the use of chemotherapy months before death is associated with terminally ill cancer patients' end of life medical care and place of death

What this study adds

The use of chemotherapy in terminally ill adult cancer patients in the final months of life is associated with increased risk of undergoing intensive medical care near death and dying in an intensive care unit

Cancer patients, caregivers, and oncologists should have a heightened awareness about the potential risks of continuing palliative chemotherapy near death

Advance care planning is needed to ensure that patients' end of life experiences are congruent with their values

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Tables

Table 1| Participants' characteristics by chemotherapy at study enrollment. Values are numbers (percentages) unless stated otherwise

Baseline characteristic*	All participants (n=386)	Before propensity weighted adjustment Chemotherapy			After propensity weighted adjustment Chemotherapy		
		Yes (n=216)	No (n=170)	P value	Yes (n=216)	No (n=170)	P value
Mean (SD) age, years	58.4 (12.5)	56.4 (12.3)	61.0 (12.5)	<0.001	57.9 (11.9)	57.9 (12.2)	>0.9
Male sex	215 (56)	119 (55)	96 (56)	0.8	(55.8)	(55.8)	>0.9
Married	236 (61)	142 (66)	94 (55)	0.04	(58.0)	(58.0)	0.8
Insured	238 (62)	145 (67)	93 (55)	0.02	(55.9)	(55.8)	0.8
Mean (SD) years of education	12.6 (4.0)	13.3 (3.9)	11.6 (4.0)	<0.001	11.9 (4.1)	11.9 (4.2)	>0.9
Race/ethnicity:				0.1			0.7
White	251 (65)	147 (68)	104 (61)		(58.7)	(58.7)	
Black	70 (18)	36 (17)	34 (20)		(22.1)	(22.1)	
Hispanic	57 (15)	26 (12)	31 (18)		(18.4)	(18.4)	
Asian	5 (1)	5 (2)	0 (0)		(0.7)	(0.0)	
Religion:				0.5			>0.9
Catholic	141 (36)	76 (35)	65 (38)		(34.6)	(34.6)	
Protestant	68 (18)	42 (19)	26 (15)		(16.0)	(16.0)	
Jewish	18 (5)	14 (6)	4 (2)		(3.4)	(3.4)	
Muslim	5 (1)	3 (1)	2 (1)		(0.7)	(0.7)	
No religion	17 (4)	8 (4)	9 (5)		(6.1)	(5.0)	
Pentecostal	9 (2)	6 (3)	3 (2)		(3.7)	(1.7)	
Baptist	58 (15)	29 (13)	29 (17)		(17.0)	(19.5)	
Institution:				<0.001			>0.9
Yale Cancer Center	75 (19)	58 (27)	17 (10)		(17.8)	(17.8)	
Veterans Affairs CCC	19 (5)	8 (4)	11 (6)		(5.7)	(5.7)	
Parkland and Simmons Cancer Center	188 (49)	106 (49)	82 (48)		(53.3)	(52.8)	
MSKCC	28 (7)	26 (12)	2 (1)		(3.3)	(3.3)	
Dana-Farber and Massachusetts General	7 (2)	3 (1)	4 (2)		(3.1)	(3.1)	
New Hampshire Oncology Hematology	67 (17)	14 (6)	53 (31)		(16.6)	(16.6)	
Cancer:				0.02			0.9
Lung	85 (22)	43 (20)	42 (25)		(23.7)	(28.2)	
Pancreatic	36 (9)	27 (13)	9 (5)		(8.4)	(8.4)	
Colorectal	57 (15)	38 (18)	19 (11)		(14.5)	(14.5)	
Other gastrointestinal	57 (15)	27 (13)	30 (18)		(13.4)	(13.4)	
Breast	42 (11)	27 (13)	15 (9)		(12.4)	(9.5)	
Other†	110 (29)	54 (25)	56 (33)		(27.5)	(27.5)	
Mean (SD) performance status‡:							
Karnofsky score	64.8 (16.2)	69.0 (14.8)	59.5 (16.4)	<0.001	64.5 (12.7)	65.3 (18.2)	0.6
ECOG score	1.7 (0.9)	1.5 (0.9)	2.0 (0.9)	<0.001	1.7 (0.7)	1.7 (0.9)	0.9
Charlson Comorbidity Index	8.3 (2.7)	7.9 (2.3)	8.8 (3.0)	0.002	8.3 (2.4)	8.3 (2.7)	0.8
Mean (SD) McGill Quality of Life§:							
Physical functioning	5.7 (2.6)	6.1 (2.4)	5.3 (2.9)	0.004	5.7 (2.3)	5.6 (3.0)	>0.9
Symptoms	5.4 (2.1)	5.8 (2.0)	4.9 (2.1)	<0.001	5.3 (1.8)	5.3 (2.2)	>0.9

Table 1 (continued)

Baseline characteristic*	All participants (n=386)	Before propensity weighted adjustment			After propensity weighted adjustment		
		Chemotherapy			Chemotherapy		
		Yes (n=216)	No (n=170)	P value	Yes (n=216)	No (n=170)	P value
Psychological:	7.2 (2.5)	7.6 (2.4)	6.7 (2.6)	0.002	7.2 (2.5)	7.2 (2.6)	>0.9
Depressed	7.4 (2.9)	7.7 (2.7)	7.0 (3.2)	0.03	6.3 (2.9)	6.3 (3.3)	>0.9
Worried	6.9 (3.2)	7.2 (3.0)	6.4 (3.3)	0.01	6.8 (3.1)	6.8 (3.6)	>0.9
Sad	7.3 (3.0)	7.9 (2.7)	6.4 (3.2)	<0.001	6.3 (3.0)	6.3 (3.1)	>0.9
Terrified	7.2 (3.1)	7.4 (2.8)	7.0 (3.4)	0.2	6.3 (2.9)	6.3 (3.5)	>0.9
Support	8.6 (1.6)	8.6 (1.7)	8.7 (1.6)	0.9	8.7 (1.6)	8.6 (1.7)	0.5
Sum score of quality of life	6.8 (1.5)	7.0 (1.4)	6.6 (1.6)	0.002	6.8 (1.4)	6.8 (1.6)	>0.9
Treatment preferences and planning:							
Wants prognostic information	269 (69)	152 (70)	117 (69)	0.8	(74.4)	(74.0)	0.9
Life extending care over comfort care	129 (31)	85 (37)	44 (24)	0.01	(29.9)	(29.1)	0.9
Chemotherapy to extend life by 1 week	288 (77)	186 (89)	102 (62)	<0.001	(79.9)	(79.2)	—
Wants to avoid dying in ICU	161 (39)	76 (33)	85 (47)	0.1	(37.4)	(37.8)	0.9
Completed living will or DPA	214 (55)	111 (51)	103 (61)	0.1	(52.5)	(53.0)	>0.9
Completed DNR order	161 (42)	77 (36)	84 (49)	<0.05	(40.4)	(40.4)	0.8
Terminal illness acknowledgment	159 (40)	76 (35)	83 (47)	0.04	(39.3)	(39.6)	>0.9
Patient-physician communication:							
Therapeutic alliance with physician	244 (64)	131 (62)	113 (67)	0.3	(64.4)	(64.6)	>0.9
Discussed end of life wishes with physician	162 (42)	80 (37)	82 (48)	0.03	(40.4)	(40.4)	>0.9
Coping style:							
Active	177 (46)	105 (49)	72 (42)	0.3	(44.7)	(47.1)	0.6
Emotional	190 (49)	106 (49)	84 (49)	>0.9	(50.0)	(48.7)	0.8
Behavioral disengagement	82 (21)	31 (14)	51 (30)	<0.001	(21.3)	(25.7)	0.3
Mean (SD) positive religious coping	11.2 (6.4)	11.3 (6.3)	11.0 (6.5)	0.6	11.4 (6.1)	11.8 (7.0)	0.6

CCC=Comprehensive Cancer Clinics; DNR=do not resuscitate; DPA=durable power of attorney; ECOG=Eastern Cooperative Oncology Group; ICU=intensive care unit; MSKCC=Memorial Sloan Kettering Cancer Center.

*Missing data: age (n=2), male sex (n=2), married (n=6), insurance (n=10), education (n=2), race/ethnicity (n=2), religion (n=2), Karnofsky score (n=20), ECOG score (n=8), Charlson Comorbidity Index (n=8), McGill Quality of Life (n=4), prognostic information (n=34), chemotherapy to extend life by 1 week (n=42), avoid death in ICU (n=40), living will or DPA (n=40), DNR order (n=38), terminal illness acknowledgment (n=40), therapeutic alliance with physician (n=31), end of life wishes (n=1), positive religious coping (n=51); multiple imputation was used to impute missing values in propensity weighted sample.

†Remaining patients had cancers that each represented ≤5% of sample.

‡Karnofsky score is a measure of functional status that is predictive of survival (0=dead and 100=perfect health); ECOG score is a measure of functional status (0=asymptomatic and 5=dead); Charlson comorbidity index is an age adjusted measure of comorbid illness (higher numbers signify greater burden).

§Subscales of McGill Quality of Life Questionnaire (scale 0-10), where 0 is undesirable and 10 is desirable; for consistency, individual items where 10 indicated undesirable states (for example, 0=not at all depressed and 10=extremely depressed) were re-scaled.

Table 2| Associations between chemotherapy at study enrollment and intensity of end of life care. Values are numbers (percentages) unless stated otherwise

Medical care in last week*	Unadjusted analysis			Propensity weighted adjusted analysis			
	Chemotherapy at enrollment		Risk difference (95% CI)	Chemotherapy at enrollment		Risk difference (95% CI)	P value
	Yes (n=216)	No (n=170)		Yes	No		
Cardiopulmonary resuscitation, ventilation, or both	30 (14)	3 (2)	12.1 (7.1 to 17.1)	24 (12)	4 (2)	10.5 (5.0 to15.5)	<0.001
Admission to intensive care unit	31 (14)	14 (8)	6.1 (−0.2 to 7.4)	26 (13)	15 (8)	5.6 (−0.5 to 11.7)	0.07
Chemotherapy	16 (7)	8 (5)	2.7 (−2.0 to 7.4)	12 (6)	10 (5)	1.1 (−3.6 to 5.7)	0.7
Feeding tube for enteral nutrition	23 (11)	9 (5)	5.3 (−0.1 to 10.7)	22 (12)	9 (5)	7.1 (1.7 to 12.5)	0.01
Hospice ≤1 week	113 (54)	61 (37)	17.6 (7.6 to 27.6)	96 (52)	70 (38)	13.6 (3.6 to 23.6)	0.008

*Missing data: admission to intensive care unit (n=1, no chemotherapy), feeding tube for enteral nutrition (n=4; n=1 chemotherapy, n=3 no chemotherapy), and hospice ≤1 week (n=12; n=8 chemotherapy, n=4 no chemotherapy).

Table 3| **Associations between chemotherapy at study enrollment, place of death, and attainment of preferred place of death. Values are numbers (percentages) unless stated otherwise**

Variable*	Unadjusted analysis			Propensity weighted adjusted analysis			
	Chemotherapy at enrollment		Risk difference (95% CI)	Chemotherapy at enrollment		Risk difference (95% CI)	P value
	Yes (n=216)	No (n=170)		Yes	No		
Place of death:							
Intensive care unit	24 (11)	4 (2)	8.8 (4.0 to 13.6)	19 (10)	7 (4)	6.1 (1.1 to 11.1)	0.02
Hospital	54 (25)	26 (15)	9.8 (1.9 to 17.8)	38 (21)	32 (17)	3.6 (−4.1 to 11.3)	0.4
Home	102 (47)	112 (66)	−18.4 (−8.7 to −28.2)	100 (52)	122 (63)	−10.8 (−1.0 to −20.6)	0.03
Inpatient hospice	28 (13)	19 (11)	−1.8 (−4.7 to −8.4)	26 (13)	22 (12)	2.0 (−4.6 to 8.7)	0.6
Nursing home	7 (3)	9 (5)	−2.0 (−6.2 to 2.1)	7 (4)	9 (5)	1.0 (−5.0 to 3.1)	0.6
Death in preferred place	140 (65)	135 (80)	−12.4 (−3.6 to −21.2)	131 (68)	154 (80)	−9.4 (−0.8 to −18.1)	0.03

*Missing data: place of death (n=1, chemotherapy), death in preferred place (n=12; n=10 chemotherapy, n=2 no chemotherapy).